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SAFELY MANAGING ACUTE OSTEOARTHRITIS IN THE EMERGENCY DEPARTMENT: AN EVIDENCE-BASED REVIEW

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☐ **Abstract—Background: Joint pain caused by acute osteoarthritis (OA) is a common finding in the emergency department. Patients with OA often have debilitating pain that limits their function and ability to complete their activities of daily living. In addition, OA has been associated with a high percentage of arthritis-related hospital admissions and an increased risk of all-cause mortality. Safely managing OA symptoms in these patients can present many challenges to the emergency provider. Objectives: We review the risks and benefits of available treatment options for acute OA-related pain in the emergency department. In addition, evidence-based recommendations will be made for safely managing pain and disability associated with OA in patients with comorbidities, including cardiovascular disease, renal insufficiency, and risk factors for gastrointestinal bleeding. Discussion: Commonly used treatments for OA include acetaminophen, oral nonsteroidal anti-inflammatory drugs, and opioids, each with varying degrees of efficacy and risk depending on the patient's underlying comorbidities. Effective alternative therapies, such as topical preparations, intra-articular corticosteroid injections, bracing, and rehabilitation are likely underused in this setting. Conclusions: Emergency providers should be aware of the risks and benefits of all treatment options available for acute OA pain, including oral medications, topical preparations, corticosteroid injections, bracing, and physical therapy. Published by Elsevier Inc.**

☐ **Keywords—arthralgia; arthritis; nonsteroidal anti-inflammatory agents; osteoarthritis**

INTRODUCTION

Osteoarthritis (OA) is a common problem, the incidence of which is increasing every day (1). By 2030, as much as 25% of the adult population is expected to have self-reported or physician-diagnosed arthritis (2). The prevalence of OA in the ambulatory care setting is approximately 3500 per 100,000 visits, where patients present most commonly with pain related to their knee, hip, and shoulder OA (3). The primary objective of the emergency provider is to rule out critical diagnoses, such as septic arthritis, fractures, and dislocations. Once this has been accomplished, however, there is still much to be done! Quality of life for this population can be dismal because of their pain (4,5). Beyond that, OA of the knee and hip joints in an ambulating population can predispose them to falls, potentially leading to intracranial hemorrhage, fractures, and other emergency conditions (6–8). How is pain and disability best managed in patients presenting with an acute

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exacerbation of their OA from the perspective of the emergency clinician?

This article will provide evidence-based recommendations to help relieve pain and suffering, minimize disability, and prevent future injury in patients presenting to the emergency department (ED) with an acute exacerbation of OA.

EPIDEMIOLOGY AND PATHOPHYSIOLOGY

There has been a significant increase in the prevalence of OA over the last 20 years, often attributed to the aging population and obesity (9). OA can be found in up to 13.9% of adults >25 years of age and 33.6% of adults ≥65 years of age (1). Perhaps more relevant in the ED, patients with OA are more likely to be admitted, have longer hospital stays, and be readmitted when compared to a similar population without OA (10). Patients with OA also have a higher risk of all-cause mortality compared to the general population and an increased level of risk that is independent of treatment complications, such as gastrointestinal (GI) bleeding from the use of nonsteroidal anti-inflammatory drugs (NSAIDs) (11,12).

The origin and progression of OA is multifactorial, including genetic predisposition, previous injuries to the joint, and other biomechanical factors (13). Many definitions for OA exist and are based on pathologic, clinical, or radiographic features, with radiographic being the most prevalent. The specifics of these classifications are complex and beyond the scope of this article. In general, OA represents degenerative changes to articular cartilage, synovium, subchondral bone, and other structures. Not surprisingly, OA symptom severity often correlates with the degree of radiographic abnormality (14,15).

An acute flare of OA commonly presents as increased pain, often associated with joint swelling, stiffness, and decreased range of motion. An acute increase in OA-related pain might be the result of trauma, overuse, or crystal formation. Many patients claim that weather changes influence their OA pain, which is supported by limited evidence (16,17).

The pathogenesis of pain in OA is complex and not clearly understood. Hyaline cartilage is avascular and not innervated by nociceptive receptors, so this is unlikely to be the source of symptoms. The sensation of discomfort is much more likely to come from synovitis, subchondral bone changes, and osteophyte formation; however, OA-related pain can be elicited over apparently normal tissue (18,19). This would indicate the possibility of central modulation of nociceptive input from the region around an arthritic joint (19).

Despite this limited understanding, several treatment options are available to the emergency provider that have shown efficacy in safely managing pain, function, and disability in patients with OA.

DISCUSSION

Oral Pharmaceutical Therapy for Osteoarthritis

Acetaminophen. A common initial choice in the management of patients with OA, acetaminophen (APAP) is thought to cause pain relief through the inhibition of prostaglandin synthesis in the central nervous system and peripheral blockade of pain impulse generation (20).

APAP has previously shown efficacy superior to placebo in treating hip and knee OA, with a number needed to treat somewhere between 4 and 16, but not superior to NSAIDs in a 2006 Cochrane review (21). Another more recent review found that APAP is not helpful in the treatment of low back pain and provides minimal short-term benefit in patients with OA (22). In 2013, because of a lack of significant benefit over placebo, the American Academy of Orthopedic Surgeons (AAOS) downgraded their guidance on the use of APAP in patients with OA of the knee to inconclusive, and no longer recommend for or against its use (23,24).

There is also evidence that unintentional overdoses of APAP occur in the elderly population and can ultimately lead to multiorgan failure and death (25). In fact, in 2011, Johnson and Johnson's McNeil Division (the manufacturer of Tylenol) changed the recommended maximum dose from 4000 mg per day to 3000 mg per day because of concerns regarding combination medications and unintentional overdose (26). While APAP is an option for the treatment of OA, it is unlikely to be as effective as other available alternatives and is not without risk.

Nonsteroidal anti-inflammatory drugs. NSAIDs provide analgesia and reduce inflammation by preventing the synthesis of thromboxanes and prostaglandins through inhibition of the cyclo-oxygenase-1 (COX-1) and COX-2 enzymes (27). These medications are generally divided into two categories: nonselective inhibitors and those that primarily inhibit the COX-2 enzyme.

The efficacy of NSAIDs in patients with OA has been clearly shown, making NSAIDs one of the mainstays of treatment with a number needed to treat between 1.6 and 3 (28,29). Nonselective NSAIDs, such as ibuprofen and naproxen, as well as COX-2 selective NSAIDs, including meloxicam and celecoxib, provide improvement in pain, function, and mobility (30). There is no evidence that the short- or long-term use of NSAIDs leads to significant changes in the progression of OA (31,32). COX-2 inhibitors are as effective as nonselective

Table 1. Risk Factors for Gastrointestinal Injury from Nonsteroidal Anti-inflammatory Drug Use

Age >65 years
A history of gastrointestinal bleeding
The use of medications, such as aspirin, warfarin, and oral corticosteroids
Serious comorbidity, including a history of myocardial infarction, chronic renal insufficiency, chronic liver disease, poorly controlled hypertension, or diabetes
Short term nonsteroidal anti-inflammatory drug use (i.e., <1 month)
The use of maximum dose nonsteroidal anti-inflammatory drugs
The presence of *Helicobacter pylori* infection

NSAIDS, more effective than APAP, and cause fewer GI complications (33). However, COX-2 selective medications tend to be more expensive than nonselective NSAIDs and are best used in patients with an increased risk of gastroesophageal reflux disease, peptic ulcer disease, and GI bleeding.

As many providers are aware, NSAIDs do not come without risks. GI bleeding, acute renal injury, and cardiovascular disease are all well recognized complications of taking NSAIDs. Despite these limitations, NSAIDs are a valuable tool in the treatment of OA. When used correctly, they can provide significant relief to the patient presenting to the ED with OA-related pain. All NSAIDs should be given at the lowest effective dose to provide the greatest benefit with the least amount of risk (30).

GI side effects and prevention. One of the most concerning potential side effects of NSAID use is injury to the upper GI tract. More than 7000 deaths and 100,000 hospitalizations in the United States each year are attributed to GI bleeding or perforation from NSAID use (34). This risk can be significant even with short-term (≤1 month) use, especially in the elderly population, with an increased relative risk of 7.2 (35). The American College of Gastroenterology (ACG) has identified multiple factors that increase the risk of GI injury from NSAID use (Table 1) (36).

The ACG has also provided excellent guidance on how to risk-stratify patients for determining how NSAIDs should be used with gastroprotective medications. High-risk patients have a history of a complicated ulcer or more than two risk factors. Patients at moderate risk have one to two risk factors, and low-risk patients have no risk factors (36). These categories are further divided by the ACG based on whether or not the patient is taking a daily low-dose aspirin for cardiovascular protection. Table 2 shows the ACG recommendations for the use of NSAIDs based on GI and cardiovascular risk.

Gastroprotective medications include proton pump inhibitors, histamine-2 receptor antagonists, and misoprostol. Histamine-2 receptor antagonists, such as famotidine, are superior to placebo but significantly less effective than proton pump inhibitors. Misoprostol is effective in preventing ulcers, but may be limited by the side effects of abdominal pain and diarrhea (36).

Cardiovascular and renal effects. All NSAIDs appear to increase the risk of myocardial infarction and death from cardiovascular disease, although naproxen appears to be the least harmful (37). Even short-term use (7–10 days), as expected from the ED, shows an increased risk of adverse events (38). These risks increase with higher doses. Naproxen causes the least amount of cardiovascular side effects, and therefore its use is recommended in patients who are taking prophylactic low-dose aspirin as noted in the ACG guidelines (39). The nonselective NSAIDs, excluding diclofenac, block the antiplatelet effects of aspirin, whereas COX-2 inhibitors do not (40,41). To prevent these potential medication interactions, aspirin should be given at least 2 hours before any nonselective NSAID.

Both classes of NSAIDs can lead to increased plasma potassium concentration and decreased renal function in patients who are taking angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (42). The risk of acute kidney injury appears to increase with combination drug therapy, specifically NSAIDs added to diuretics and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (43). This increased risk ratio was 1.31 relative to patients only taking one antihypertensive combined with NSAIDs.

Opioids. Opioid pain medications, not including tramadol, have a modest effect on OA-related pain but put patients at higher risk for adverse events. A Cochrane

Table 2. American College of Gastroenterology Recommendations for Prevention of Injury to the Upper Gastrointestinal Tract with Oral Nonsteroidal Anti-inflammatory Drug Use

	Low GI Risk	Moderate GI Risk	High GI Risk
Low CV risk	NSAID	NSAID plus GP medication	Alternative therapy or COX-2 inhibitor plus GP medication
High CV risk*	Naproxen plus GP medication†	Naproxen plus GP medication†	Alternative therapy, avoid all oral NSAIDs

COX-2 = Cyclo-oxygenase-2; CV = cardiovascular; GI = gastrointestinal; GP = gastroprotective; NSAID = nonsteroidal anti-inflammatory drug.
* High CV risk indicates the patient takes a daily low-dose aspirin for cardiovascular protection.
† Aspirin should be taken at least 2 hours before naproxen.

review from 2014 showed a pool risk ratio of 1.49 for any adverse event and 3.35 for serious adverse events (44). In an elderly population, opioid pain medication has been shown to increase the risk of fractures and all-cause mortality compared to NSAIDs (45). Higher doses of opioids lead to a higher risk of fracture risk (45,46). These same studies note an increased risk of GI bleeding with opioids compared to COX-2 inhibitors.

Tramadol, a weak opioid that also inhibits the reuptake of serotonin and norepinephrine, has a small but significant effect on OA-related pain (47). It also is effective as an add-on therapy for patients who are already taking NSAIDs (48,49). In patients with OA, tramadol has a number needed to treat for moderate clinical improvement of 6 and a number needed to harm of 8 for adverse effects, such as nausea, dizziness, and headache (49). Caution should still be taken because elderly patients who are taking tramadol have a higher fracture risk than the general population, and may even have a similar fall risk to that found with other opioids (50,51). Overall, the published literature supports the use of tramadol over traditional opioids for acute OA-related pain relief.

Corticosteroid Injection Therapy

Corticosteroids are often used in orthopedic, sports medicine, and primary care clinics to provide relief for various sources of musculoskeletal pain. Depending on the etiology of the patient's pain, they can be administered around tendons or intra-articularly. In the case of symptomatic OA, injections are typically placed in the intra-articular space.

The most likely location for this to be considered in the ED is the knee (because it is the most common location of OA), although glenohumeral, femoroacetabular, and carpometacarpal locations may be considered, depending on the situation (52–55). Systematic reviews show a clinically significant reduction in OA-related knee pain, but not function, within 1 week after corticosteroid injection with a number needed to treat of 3 to 4 (56,57). These reviews also show a superior effect for triamcinolone compared to other injectable corticosteroids. It is important to note that the pain relief experienced by a patient that responds to the injection can be expected to last approximately 4 to 6 weeks (58). This pain relief is significant, especially in an elderly patient who is already at risk of falling and in whom a narcotic pain medication could lead to a debilitating injury (59).

One potential concern in administering intra-articular steroids is their effect on the surface of the joint—and, in addition, the effect of the coadministered anesthetic. However, several studies have shown no clear association between intra-articular corticosteroid injections and joint degeneration, including some studies that involved patients with rheumatoid arthritis receiving as many as 10 injections per year (60–62). There is some evidence, at least in patients with rheumatoid arthritis, that the suppression of inflammation by these injections may actually protect the joint (63).

A local anesthetic, typically lidocaine, is often coadministered with the corticosteroid for diagnostic and therapeutic purposes. In vitro studies have shown significant damage to chondrocytes with prolonged exposure to these anesthetics (64,65). There is also some evidence to suggest that even short-term exposure to local anesthetics is toxic to chondrocytes (66,67). In spite of this evidence, there is no definitive in vivo data to suggest that a single dose of local anesthetic would lead to any long-term cartilage damage, and providers should consider the addition of a local anesthetic as indicated for diagnostic or therapeutic purposes.

The dose of triamcinolone most commonly cited in OA of the knee is 40 mg intra-articularly, administered no more often than every 3 months (61,68). This time period deserves special consideration in patients who are scheduled to undergo total knee arthroplasty. Recent evidence suggests that intra-articular corticosteroid injections may increase the risk of postoperative infection, and ED providers should therefore have a discussion with an orthopedic expert before injecting this patient population (69).

The intra-articular knee injection—likely the most common intra-articular injection to be used in the ED—can be safely and effectively approached in most patients using a seated technique. After appropriate skin preparation using betadine or other sterile preparation, the needle is placed just lateral to the patellar tendon and directed toward the center of the joint space, at roughly a 45° angle medial to the skin (Figure 1). The needle is then advanced into the intra-articular space posterior to the patellar tendon. There should be little resistance to both advancing the needle and to the actual injection of medication. No bone or cartilage should be contacted with this approach.

It is important for both the provider and the patient to understand the potential risks and benefits of a corticosteroid injection. Diabetics can expect impaired glucose control and should monitor their glucose levels closely for up to 4 days (70). Injections near the surface of the skin may cause fat atrophy and hypopigmentation (71). Intratendinous or peritendon injections increase the risk of tendon rupture (72,73). Infection is a risk any time an intra-articular procedure is performed. For intra-articular injections, historical infection rates are as low as 6 in 100,000 people (74). The contraindications to corticosteroid injections include cellulitis at the

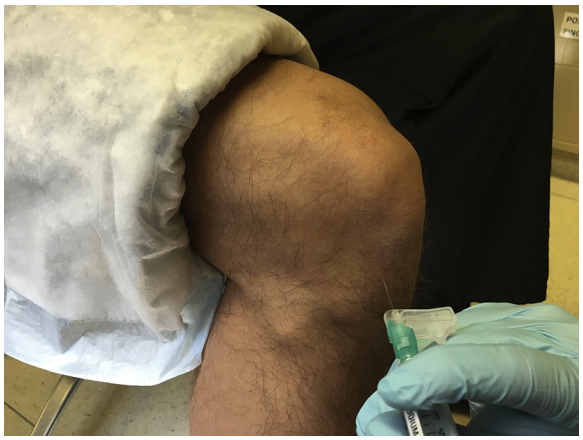

Figure 1. Location and positioning for anterolateral approach of an intra-articular knee injection.

injection site, known allergy or hypersensitivity to the corticosteroid, and septic arthritis.

Some cases may present with features that are concerning for septic arthritis. In these cases, the emergency provider should aspirate intra-articular fluid first and obtain testing for features of infection before injecting a corticosteroid. While this process requires two separate intra-articular procedures, it avoids the inappropriate injection of steroids into an infected joint.

Other Therapy Options

Topical NSAIDs. Oral NSAIDs have long been the mainstay of pharmacologic therapy in patients with OA. As discussed above, these medications can carry cardiovascular, renal, and GI risks that must be considered. Another excellent option—especially for patients who are at high risk for complications with oral NSAID use—is a topical NSAID. Topical formulations have shown significantly lower risk when compared with oral NSAIDs (75–77).

In the United States, several topical NSAID preparations are available for treating OA-related pain, including diclofenac sodium 1% gel (Voltaren Gel; Endo Pharmaceuticals, Malvern, PA), diclofenac sodium topical solution 1.5% in 45.5% dimethyl sulfoxide (Pennsaid; Mallinckrodt, Inc., Saint Louis, MO), and diclofenac epolamine 1.3% (Flector Patch; Alpharma Pharmaceuticals LLC, Piscataway, NJ) (78). These medications have shown the ability to improve symptoms and quality of life comparable to oral NSAIDs, with a number needed to treat of 6 (79–81). Topical NSAIDs are typically more expensive in the United States than oral formulations and may cost between $50 and $300 for a full course of treatment, depending on the product. This may be prohibitive to some patients.

Topical NSAIDs appear to be the most efficacious for hand and knee OA (82). The AAOS and American College of Rheumatology consider topical NSAIDs to be first-line options for the treatment of OA of the knee (83). In general, topical preparations provide a safe and effective alternative to oral NSAIDs, especially in those that are at higher risk of adverse effects.

Other topical agents. Topical treatment of OA is not limited to NSAIDs. Topical capsaicin can be considered for the knee and hand, and may be effective for up to 20 weeks (25). Of note, however, is the fact that topical capsaicin does increase the risk of skin irritation local to the site of application (84). The transdermal 5% lidocaine patch may also be a reasonable option for patients with an acute exacerbation of knee OA (85).

Glucosamine. Studies have found glucosamine to be safe but largely ineffective for pain relief (86,87). However recent research indicates it may have an impact on the progression of OA (88). In spite of this, glucosamine has limited utility in the treatment of patients who present to the ED for the treatment of acute joint-related pain.

Heat and cold therapy. Cold therapy improves range of motion, function, and strength compared to heat and placebo (89). There is even some concern that elevated intra-articular temperatures through heat application may increase damage to the inflamed arthritic joint (90). Cold therapy should be recommended over heat in acute OA-related complaints.

Bracing and physical therapy. Several types of bracing are available, from simple sleeves and cockup wrist splints to complex valgus knee braces. Flexible knee sleeves, made from cotton, neoprene, nylon, or other materials, can provide pain relief and possibly improve balance in patients with OA of the knee (91,92). Prefabricated and custom splints can reduce pain and disability in patients with carpometacarpal OA (93,94).

Patients with OA generally benefit from range of motion and strengthening exercises (95,96). Complete immobilization should be reserved only for those patients with severe symptoms and should be discontinued as soon as possible, ideally within 5 to 7 days. This must be made clear to the patient, especially those that are unlikely to have follow-up appointments within 1 to 2 weeks.

Physical therapy has been shown to be of significant benefit in many types of OA (97–99). Unfortunately, it is uncommon and often impractical for the emergency clinician to provide a direct referral to physical therapy or other rehabilitation service. In spite of this, it is important that the emergency provider explain the benefits of therapy to the patient verbally and through discharge instructions so that they may pursue such

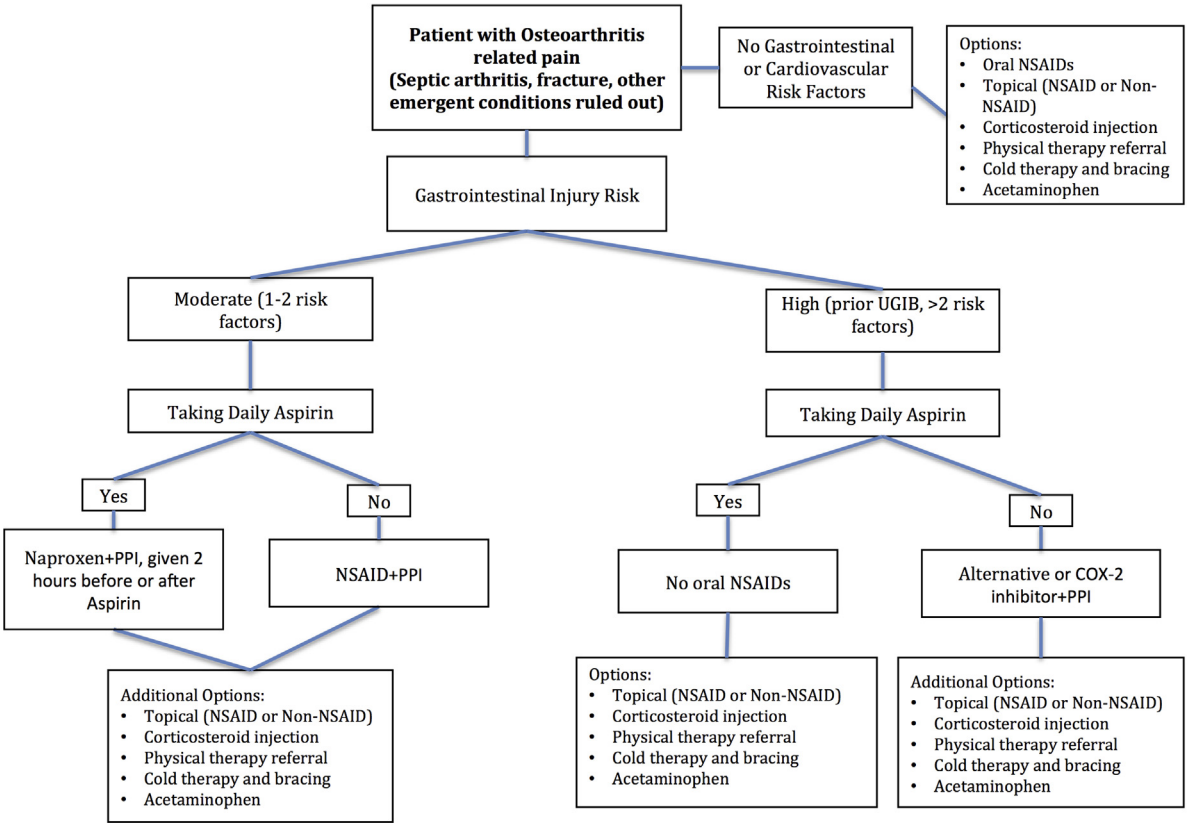

Figure 2. Algorithm for managing osteoarthritis in the acute setting. NSAID = Nonsteroidal anti-inflammatory drug; PPI = proton pump inhibitor; UGIB = upper gastrointestinal bleed.

treatment via other avenues, mainly their primary care provider. If the emergency clinician has the ability to directly refer these patients to therapy or rehabilitation services it should be seriously considered, especially in those patients who have presented to the ED multiple times with the same OA-related complaint.

PUTTING IT ALL TOGETHER

The first step in evaluating a patient presenting to the ED with an acute or chronic complaint of joint-related pain is to evaluate for an emergent condition. The differential diagnosis includes septic arthritis, fracture, gout, and tendon or ligament injury. Once these or other concerning conditions have been ruled out and the clinician plans to treat the patient for an acute or chronic exacerbation of OA, the next step in determining the safest and most effective treatment is to determine the patient's level of GI and cardiovascular risk (Figure 2). When indicated, oral NSAIDs should always be given at the lowest effective dose; opioid medications, preferably tramadol, should only be used in circumstances when no other reasonable options are available. Topical therapy is an effective treatment option for knee- and hand-related complaints. Intra-articular corticosteroid injections are a safe alternative for many cases of acute OA-related pain, especially in the knee, and should be considered. When feasible, rehabilitation or physical therapy referral should be exercised in this patient population.

CONCLUSION

Through careful selection from the many treatment options available, the emergency clinician can provide safe and effective pain relief without added risk to the patient presenting to the ED with an acute exacerbation of OA.

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ARTICLE SUMMARY

1. Why is this topic important?

Acute osteoarthritis pain is common in patients presenting to the emergency department. Side effects of common methods of managing osteoarthritis pain include an increased risk of cardiovascular complications, gastrointestinal bleeding, and falls.

2. What does this review attempt to show?

This review evaluates the safety and efficacy of the many treatment options available for managing osteoarthritis-related pain.

3. What are the key findings?

Nonsteroidal anti-inflammatory drugs can be used safely in many patients with gastrointestinal bleeding and cardiac risk factors, as long as the appropriate medications are selected. Corticosteroid injections are not harmful to the joint and provide significant short-term pain relief. Multiple effective nonstandard options are available to treat patients with osteoarthritis pain, such as topical preparations, bracing, and physical therapy.

4. How is patient care impacted?

Safer management of acute osteoarthritis pain can help to prevent complications and provide better symptom relief.